Remarks

The Office Action mailed April 5, 2004, has been received and carefully reviewed. Upon entry of the present amendment canceling claims 1-39, 41, 45, 47, 51, 56 and 70-73, without prejudice, and amending claims 40, 42, 46, 48, 52-55, 57 and 61-64, the pending claims are claims 40, 42-44, 46, 48-50, 52-55 and 57-69. Reconsideration and withdrawal of the rejections, and allowance of the pending claims, is respectfully requested.

Amendment of claims 40, 46, 52-55 and 61-63 to recite glycosylphosphotidylinositol anchor attachment site, or an immunogenic fragment of said polypeptide is found, for example, at page 45, line 20 ("GPI-anchor cleavage/attachment site"); page 82, line 16 ("GPI anchor addition sites"); and page 21, lines 12-15 (immunogenic fragments) of the specification.

Rejection under 35 U.S.C. §112, First Paragraph

The Examiner has maintained the rejection of claims 40-69 under 35 U.S.C. §112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to make and use the invention commensurate in scope with the claims. This rejection is respectfully traversed.

The Examiner states that the specification, while being enabling for therapeutic immunization comprising a vector which encodes TSA-1, does not reasonably provide enablement for a therapeutic immunization with "any" polypeptide. Applicants disagree. Even before the amendment submitted herewith, the claims under examination did not recite immunization with "any polypeptide", but recited a defined class of immunogenic polypeptide which was associated with a protozoan cell surface or secreted. Moreover, in order to advance prosecution, the claims are amended herewith to recite that the immunogenic polypeptide comprises a *Trypanosoma* polypeptide comprising a glycosylphosphotidylinositol anchor attachment site, or an immunogenic fragment of said polypeptide.

It is respectfully submitted that the specification enables treatment of a *Trypanosoma* infection by administering a multicomponent vaccine comprising an immunogenic polypeptide and/or a polynucleotide encoding an immunogenic polypeptide, wherein the immunogenic

polypeptide comprises a *Trypanosoma* polypeptide comprising a *glycosylphosphotidylinositol (GPI) anchor attachment site*, or an immunogenic fragment of said polypeptide. For example, *T. cruzi* polypeptides anchored by GPI are immunogenic:

> The majority of surface proteins in trypomastigotes and amastigotes of *T. cruzi* are GPI-anchored and many of these surface proteins both elicit and are bound by antibodies. In addition, the GPI anchoring mechanism in *T. cruzi* appears to be very sloppy with a significant portion of proteins targeted for GPI addition being secreted without the addition of a GPI anchor (N. Garg et al., J. Biol. Chem. 272:12482-12491 (1997)). In the case of amastigotes, these secreted proteins lacking GPIs enter the host cell cytoplasm, are presented by class I MHC molecules and elicit the production of CTL responses. On extracellular amastigotes and trypomastigotes, these same proteins in a surface-anchored form sensitize parasites to detection by antibodies specific for the proteins. Lastly, significant class II MHC-restricted, $CD4^+$ T cell reactivity is elicited by GPI-anchored proteins. Thus GPI anchored proteins appear to be excellent targets for stimulation of protective antibody, Th1-biased $CD4^+$ T cell responses, and $CD8^+$ T cell responses (specification at page 13, line 19; bridging to page 14, line 2).

C-terminal GPI-anchor cleavage/attachment sites are also taught by the specification at page 45, line 20, and at page 82, line 16.

In addition, the Examiner is incorrect in stating that the sole working example is that of the antigen TSA-1. To the contrary, the specification contains working examples showing successful immunization of mice using a polynucleotide encoding *T. cruzi* TSA-1 (Example I); a polynucleotide encoding *T. cruzi* ASP-1, ASP-2 or TSA-I, (or combination of all three) (Example II); and a polynucleotide encoding immunogenic fragments of *T. cruzi* ASP-1, ASP-2 or TSA-I (or combination of all three) (Example IV). ASP-1, ASP-2 and TSA-1 are polypeptides from the trans-sialidase family of proteins (e.g., specification at page 25, lines 4-5), and all contain GPI attachment sites (e.g., specification at page 13, lines 5-6). It is respectfully submitted that the claims, as amended, are commensurate in scope with Applicants' teachings.

At page 4 of the Office Action mailed April 5, 2004, the Examiner appears to allege that, in addition to enablement, the written description requirement of 35 U.S.C. §112, first paragraph, is not met. Specifically, the Examiner states that Applicants' specification has not provided

guidance as to which of the multitude of protozoan polypeptides "associated with the cell surface or secreted" are capable of eliciting this immunoprotective response, and that a specification offers a "mere statement that a multitude of proteins are part of the invention" does not offer guidance beyond the antigen TSA-1. Applicants disagree.

First, as noted above, the claims now recite, as the immunogenic polypeptide, a *Trypanosoma* polypeptide comprising a *glycosylphosphotidylinositol (GPI) anchor attachment site*, or an immunogenic fragment of said polypeptide. The specification at page 13, line 17; bridging to page 14, line 2 above, provides clear guidance that *Trypanosoma* polypeptides with GPI attachment sites are immunogenic. This is much more than a "mere statement that a multitude of proteins are part of the invention" and serves as clear guidance to one of skill in the art. Additionally, working examples involving TSA-1, ASP-1 and ASP-2, alone or in combination. Applicants submit that the specification offers guidance well beyond just the antigen TSA-1, and that the written description requirement is satisfied for the claims as amended.

Reconsideration and withdrawal of the rejections of claims 40-69 under 35 U.S.C. §112, first paragraph, is respectfully requested.

Rejection under 35 U.S.C. §102

The Examiner maintained the rejection of claims 61-64 under 35 U.S.C. §102(a) as being anticipated by Wizel et al. (Infection and Immunity, Vol. 66, No. 11, November 1998, pp. 5073-5081). This rejection is respectfully traversed.

Claims 61-64 recite a multicomponent vaccine *comprising a plurality of components selected from the group consisting of* (a) an immunogenic polypeptide and (b) a polynucleotide comprising a nucleotide coding region encoding an immunogenic polypeptide. The multicomponent vaccine must contain, at a minimum, two immunogenic polypeptides, two polynucleotides, or one of each in order for it to contain a plurality of components selected from the group consisting of (a) and (b). The Examiner states that the second component in the "multicomponent vaccine" taught in Wizel et al. is a carrier. A carrier may be a general

"component" of a vaccine but it is *not* an immunogenic polypeptide or a polynucleotide comprising a nucleotide coding region encoding an immunogenic polypeptide, as recited in (a) or (b) of claims 61-64 and thus cannot qualify as the "second" component in the vaccine as recited in claims 61-64. As such, Wizel et al. teach a vaccine with only one "component" as recited in claims 61-64 and this teaching does not anticipate those claims.

The Examiner maintained the rejection of claims 61-64 under 35 U.S.C. §102(a) as being anticipated by Costa et al. (Vaccine, Vol. 16, No. 8, 1998, pp. 768-774) for similar reasons as the rejection based on Wizel et al., alleging that the second "component" of the vaccine is an adjuvant. This rejection is respectfully traversed.

An adjuvant may be a general "component" of a vaccine but it is *not* an immunogenic polypeptide or a polynucleotide comprising a nucleotide coding region encoding an immunogenic polypeptide thus cannot qualify as the second component in the vaccine as recited in claims 61-64. As such, Costa et al. teach a vaccine with only one "component" as recited in claims 61-64 and does not anticipate those claims.

The Examiner maintained the rejection of claims 61-64 under 35 U.S.C. §102(b) as being anticipated by Reed (U.S. Patent No. 5,304,371) for similar reasons as the rejection based on Wizel et al., alleging that the second "component" of the vaccine is Freund's adjuvant. This rejection is respectfully traversed.

Again, Freund's adjuvant may be a general "component" of a vaccine but it is *not* an immunogenic polypeptide or a polynucleotide comprising a nucleotide coding region encoding an immunogenic polypeptide thus cannot qualify as the second component in the vaccine as recited in claims 61-64. As such, Reed teach a vaccine with only one "component" as recited in claims 61-64 and does not anticipate those claims.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §102 is respectfully requested.

Rejection 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 40-69 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner stated that the recitation of "associated with a protozoan cell surface" renders the claims vague and indefinite.

This rejection is respectfully traversed; however, the claims have been amended to delete recitation of "associated with a protozoan cell surface" thereby rendering the rejection moot.

Reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph, is respectfully requested

Summary

It is respectfully submitted that the pending claims 40, 42-44, 46, 48-50, 52-55 and 57-69 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to **Mail Stop AF**, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 2 day of June, 2004, at 3:45 pm (Central Time).

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